Development of two-doses viral-vectored malaria vaccine based on heterologous prime-boost regimen

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Our malaria vaccine is designed to be administered to infants and young children under the age of 5, the group with the highest malaria mortality rate, and its success would make a significant contribution to international health care. Furthermore, it would serve as a "shield of epidemic prevention" for the Japanese population as a powerful vaccine platform, proven to be effective and safe for combating severe pediatric infectious disease outbreaks in the country. The advantages of the LC16m8Δ/AAV1 vaccine include: i) It can induce a strong cellular immune response, far surpassing recombinant protein vaccines. ii) LC16m8Δ is very cost-effective to manufacture. iii) It can be stored and preserved at room temperature without the need for a cold chain. On the other hand, there is a concern regarding the "potential disadvantage" of viral vectors, where pre-existing immunity to the vector might reduce the vaccine's efficacy (vaccine breakthrough). For the vaccinia vector MVA, it has been reported that vaccination in individuals with pre-existing immunity does not impair its effectiveness. There is limited knowledge on the development of vaccines using AAV vectors. In AAV gene therapy research, it has been reported that high-dose intravenous administration to individuals with pre-existing AAV neutralizing antibodies leads to reduced efficacy and liver damage due to the high dose. In contrast, our AAV1 dose is very low, about 1/500 to 1/1,000 of the gene therapy research dose, and is administered via intramuscular injection. This is expected to have low invasiveness, with a very low likelihood of interference or adverse reactions. In this study, we will create an animal model with pre-existing immunity and transition antibodies to LC16m8Δ/AAV1, demonstrating that vaccine efficacy is maintained even in individuals with pre-existing antibodies, thus achieving non-clinical POC. The "Malaria Vaccine for African Children" that we are proposing targets children under the age of 5. The domestic Phase 1 trial is expected to be conducted on Japanese adults (aged 18-40), where pre-existing smallpox antibodies are not anticipated. Since 20-30% of Japanese women in their 20s-40s carry neutralizing antibodies against AAV1, it is possible that infants may also have maternal transition antibodies. To provide a beneficial vaccine platform accessible to many Japanese citizens (in line with the SCARDA project objectives), it is important to consider expanding the target population to include those with pre-existing immunity or transition antibodies. This project will also demonstrate that the vaccine platform is a versatile, re-administerable new modality.